REFLUX NEPHROPATHY

ESSAY

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UROLOGY

BY

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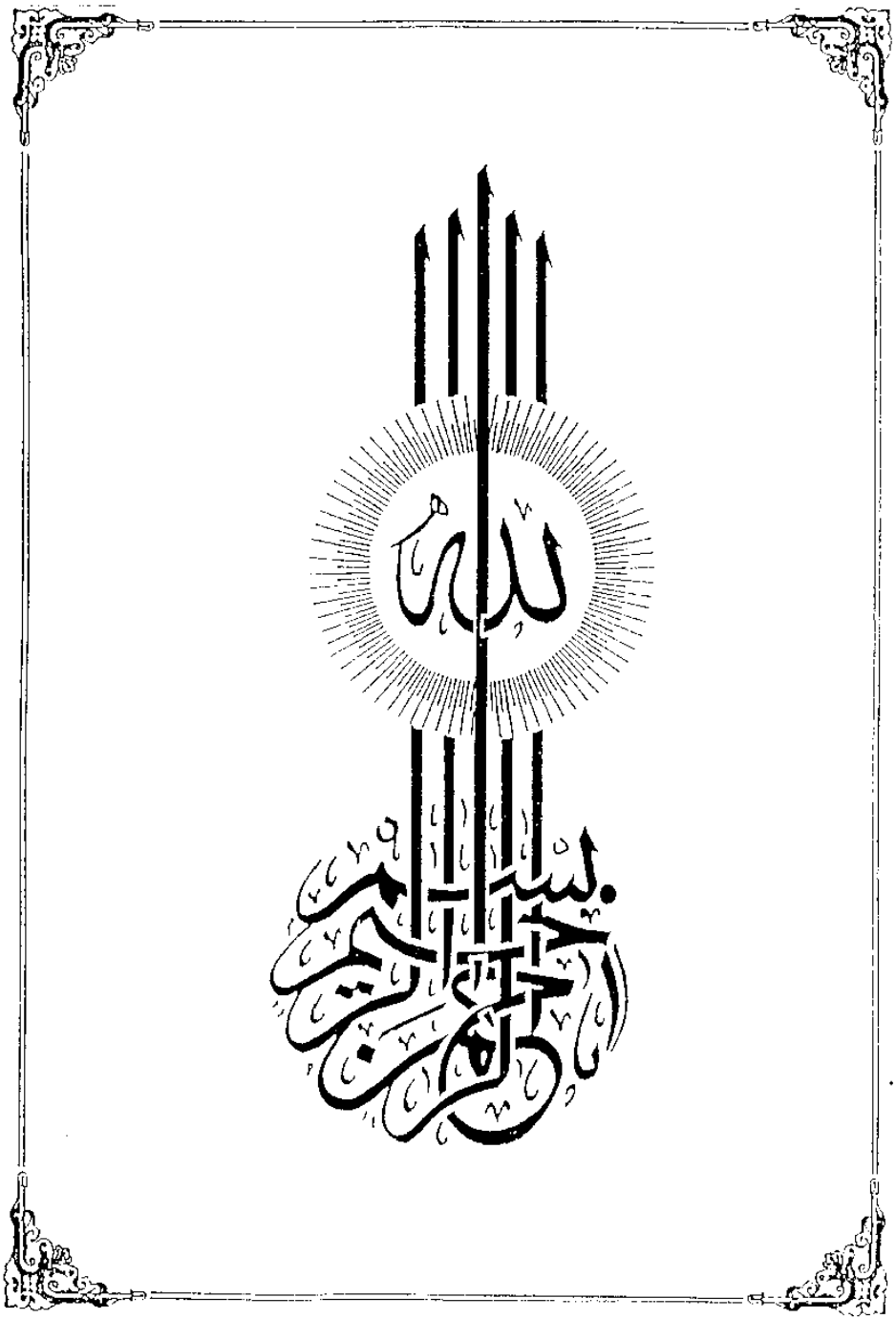
R.A.A.Al-DEEB



بسم الله الرحمن الرحيم

﴿ سنريهم آياتنا في الآفاق وفي أنفسهم حتى يتبين لهم أنه الحق من ربهم أو لم يكف بربك أنه على كل شيء شهيد ﴾

[صدق الله العظيم]

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TO MY PARENTS

WITH LOVE AND AFFECTION

INTRODUTION

INTRODUTION

INTRODUCTION

Sembl:now observed reflux of urine stained with methylene blue from the bladder into the ureters of both dogs and rabbits in 1883. Pozzi reported the first case of vesicoureteral reflux in humans in 1893. He noted the appearance of urine from the distal end of a ureter divided during a transabdominal gynecologic procedure. In experiments with human cadavers, young was unable to make urine flow backward from the bladder into the ureter, irrespective of the pressure used in filling(1898). In 1929, Gruber noted that the structure of the trigone and ureterovesical junction varied in different animal species and that the incidence of vesicoureteral reflux varied directly with the length of the intravesical ureter and the muscular development of the trigone. Kretschmer (1916) and Bumpus (1924) presented early observations on the clinical use of cystography and the occurrence of vesicoureteral reflux.

Partly because reflux is normal in many mammals, its presence in humans was not always considered to be abnormal until Hutch (1958) convincingly demonstrated that acquired periureteral diverticula commonly resulted in reflux, which led to renal damage from hydronephrosis or supraimposed infection. The cystogram came into general use as a clinical tool through the 1950's, and with it the recognition that reflux was not uncommon and had several specific causes. King and Levitt 1986.

Reflux nephropathy is defined as renal scarring associated with vesicoureteral reflux, and consists of calyceal clubbing or deformity with overlying corticomedullary scarring (Lerner, et al,. 1987) . Vesicoureteral reflux is aco-

ndition in which the bladder contents enter the ureters retrogradely through an incompetent ureterovesical junction Shafir, et al. 1982. Renal scarring refers to that spectrum of radiographic changes in the kidney often referred to as chronic pyelonephritis (Woodard and Rushton, 1987). The deleterious effects of infected urine refluxing into the collecting system are well documented. The resultant renal scarring, parenchymal atrophy, interference with renal growth and function, and associated hypertension are recognized sequelae (Kogan, et al,. 1986) . Although the aetiology and pathogensis of reflux nephropathy remain controversial it is generally agreed that early accurate identification of reflux and appropriate management with continuous antibiotic chemoprophylaxis or, when necessary, surgical correction may alter the course of this disease and reduce the amount of damage inflicted upon the kidney(Jerkins and Noe, 1982).

The true incidence of vesicoureteral reflux is not known since most patients diagnosed present with urinary tract infection where as others with vesicoureteral reflux alone go undetected. One to two per cent of prepubertal children have bacteriuria on screening ; 14 to 35 per cent of these will have vesicoureteral reflux. Of children who present with symptomatic urinary tract infection 18 to 50 per cent will have vesicoureteral reflux. Baily (1978) found that o.4 to 1.8 per cent of healthy subjects in early childhood had vesicoureteral reflux. 10 per cent of healthy neonates with negative urine cultures were found to have vesicoureteral reflux. (Lerner. et al 1967)

A symptomatic urinary tract infection will occur in about 3 per cent of female and 1 per cent of male children. In addition, asymptomatic or covert infection occurs in bet-

ween 1 and 2 per cent of school-aged girls at any given time however, is rare in boys. Radiologic studies on children with symptomatic or asymptomatic urinary tract infection reveal the presence of vesicoureteral reflux in 25 to 50 per cent of the cases . When pyelonephritic scarring is found on the excretory urogram (IVP) the incidence of reflux rises to over 90 per cent . That the incidence of vesicoureteral reflux appears to be inversely related to age, reflects the tendency for primary reflux to resolve spontaneously as the intramural ureteral tunnel elongates with the child's growth and maturation. For instance, reflux has been reported to occur in 47 to 57 per cent of neonates with urinary infection . (Woodard and Rushton 1987) . The preschool child suffers the greatest incidence of urinary tract infection, reflux and urosepsis have an identical ratio in the female and male child 9:1 and reflux and infection in the bladder are inseparable .(Howerton and Lich 1963).

Siblings of patients with reflux have a much higher incidence of reflux than that expected in the general population. Siblings of patients with reflux and radiographic evidence of renal damage are not only at higher risk for reflux than the general population but also have a higher incidence of established renal damage. (Jerkins and Noe 1982).

The incidence of the orifice which allows reflux parallels the incidence of other congenital anomalies which are transmitted by polygenic inheritance. Such well-known congenital, familial and hereditary disorders as cleft lip with or without cleft palate. These abnormalities have multifactoral and polygenic inheritance patterns, that is multiple environmental influences and multiple genes are operative .

It also has been demonstrated that the risk of a first - degree relative (parent, sibling, offspring) having one of these defects is 8 to 10 times greater than an unrelated individual in the general population. (Burger and Smith 1971). Mebust (1972) found that concomitant vesicoureteral reflux occurs in identical twins .

EMBRYOLOGY, ANTATOMY AND PHYSIOLOGY

OF THE URETEROVESICAL JUNCTION

EMBRYOLOGY OF THE URETEROVESICAL JUNCTION

Development of the ureter

The ureteral bud originates from the mesonephric duct after 28 days of development. The ureteral bud then simply elongatesas a hallow tube to ascend the pelvis. Between 28 and 35 days of development, the ureter is patent in its entire length . This patency may relate to the hydrostatic pressure generated by mesonephric urine, which fills the ureter since the cloaca is still imperforate at this stage. Intense elongate growth of the ureter may obliterate the lumen. The lumen extends cranially and caudally from the midportion of the ureter. By 8 weeks of development the ureter is a patent tube without muscle that has elongated pari passu with ascent of the kidney. After 10 weeks the epithelium of the ureter becomes two-layered and by 14 weeks a transitional epithelium has appeared. By 18 weeks the ureter demonstrates relative intrinsic narrowings at the ureteropelvic junction, pelvic brim, and ureterovesical junction, and complementary intrinsic dilalations of the upper, middle, and lower spindles of the ureter. However, the ureter may elongate in excess of that needed to accompany ascent of the kidney. To absorb the excess length, the ureter may become tortuous or invaginate its wall as pleats, the"fetal folds" of ostling. Smooth muscle of the ureter first appears at the extravesical ureter after about 14 weeks; mmascularization gradually extends toward the kidney and is completed by about 18 weeks. By 36 weeks the muscle coat of the intravesical ureter is complete. Postnatally, the infant's growth rate exceeds that of the ureter. The ureter may lose its tortuosity and unfolds its pleats. The pleats are not ordi-

narily obstructive. However, a pleat that intrudes into the lumen of the ureter and that is fixed by adventitia of the ureter may obstruct urine drainage as a valve.

Development of the trigone and bladder:

By 28 days of development, the mesonephric ducts have already reached and fused with the urogenital sinus. This fusion involves the coalescence of the epithelium of the urogenital sinus (endoderm derivative) with that of the mesonephric duct (mesoderm derivative) . The segment of the mesonephric duct distal to the site of origin of the ureteral bud dilates as the common excretory duct, the precursor of the trigone. The common excretory duct is absorbed into the urogenital sinus either directly or after the terminus of the duct loops. After the right and left common excretory ducts have been absorbed into the urogenital sinus, the epithelia of the ducts fuse toward the midline as a triangular area, the primitive trigone. The terminus of the ureter enters the bladder directly. The separate development of the trigone and bladder may account for the fact that the muscle laminae of the trigone are contiguous with the muscle of the ureter and not with the bladder detrusor. This separate development may also account for pharmacologic responses of the musculature of the bladder neck and trigone, which differ from those of the bladder detrusor. The mesenchyme of both common excretory ducts is believed to migrate toward each other, since the endodermal mucosa of the bladder does not persist in the midsection of the trigone. The mesonephric ducts also migrate caudally and flank the paramesonephric ducts at the level of the urogenital sinus. This is the site of the future verumontanum . The period wher the ureter